# Stressful Life Events and Anxiety, Depression, and Fatigue in People with Initial Central Nervous System Demyelination.

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I declare that this research report is my own original work and that, to the best of my knowledge and belief, it does not contain material from published sources without proper acknowledgement, nor does it contain material which has been accepted for the award of any other higher degree of graduate diploma in any university.

*Signature*: ……  *Date*: ……

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# Stressful Life Events and Anxiety, Depression, and Fatigue in People with Initial Central Nervous System Demyelination.

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Abstract

There is no known cure for Multiple Sclerosis (MS), a chronic inflammatory disease characterised by demyelination of the central nervous system. Current treatment recommendations focus on symptom management. In order to inform recommendations there is a need to identify factors that exacerbate MS symptoms. Stress has consistently been associated with MS relapse, however few studies have examined the impact of stress on other MS symptoms. This study investigated the association between various measures of stressful life events and other MS symptoms implicated in the progression of the disease, which include anxiety, depression, and fatigue. The 236 participants (184 females) with a first clinical diagnosis of demyelination participated in annual reviews for five years. Measures of stressful life events, anxiety, depression, and fatigue were obtained. As predicted the results showed negative, but not positive, stressful events were associated with anxiety, depression, and fatigue. Consistent with hypothesis two, an increased number of stressful events that were perceived as more severe and had a higher readjustment weighting were significantly associated with anxiety and depression. More negative events that had a higher readjustment weighting, but not perceived severity, were associated with fatigue. Contrary to the third hypothesis, an increased duration of negative stressful events were significantly associated with anxiety and depression but not fatigue. Overall, these findings indicate negative stressful events, but not positive stressful events, are associated with subsequent anxiety, depression, and fatigue in people with MS. Importantly various aspects of stress were shown to affect anxiety and depression differently to fatigue.

Experiencing stress or interpreting events as stressful almost universally has negative effects on health (Schneiderman, Ironson, & Siegel, 2008). Multiple Sclerosis (MS), a chronic inflammatory disease characterised by demyelination, is no exception to these effects. As there is no known cure for MS, current treatment recommendations focus on the management of symptoms (Broadley et al., 2014). Thus there is a need to identify factors that exacerbate MS symptoms in order to inform effective treatment recommendations. Individuals with MS believe stress is one of the most common factors that exacerbate their symptoms (Heesen et al., 2007). The majority of research supports this notion, and the results of these studies have shown a consistent association between stressful life events and subsequent relapses in MS (Artemiadis, Anagnostouli, & Alexopoulos, 2011; Mohr, Hart, Julian, Cox, & Pelletier, 2004). However, relapses are a short-term outcome which are not indicative of overall disease progression (Confavreux, Vukusic, Moreau, & Adeleine, 2000). Further, there are limited studies that have examined the association between stressful life events and other MS symptoms. Therefore, the aim of this study was to go beyond the examination of relapses and investigate the association between different components of stressful life events (number, severity, and duration) and other MS symptoms implicated in the progression of the disease, which include anxiety, depression, and fatigue.

**Multiple Sclerosis**

Multiple Sclerosis is a chronic inflammatory disease that is characterised by the demyelination of axons of the central nervous system (Compston & Coles, 2008). Demyelination refers to the process by which the insulating covers or myelin sheaths of axons degenerate (Song et al., 2005). This degeneration reduces the effectiveness of communication of the nervous system, which results in a range of

symptoms. These commonly include muscle weakness or spasms, visual problems, fatigue, depression, and anxiety (Compston & Coles, 2008). To be diagnosed with MS, an individual generally needs to experience two episodes of demyelination. After the first episode of demyelination, approximately 80% of individuals experience further episodes and develop MS after 5 years (Weinshenker et al., 1989). Within western countries approximately 1 in 1000 people are affected by MS (Sadovnick & Ebers, 1993) including more than 22,000 Australians (Palmer et al., 2013), with recent research indicating the prevalence of the disease is increasing (Simpson et al., 2011).

The progression of MS can take a number of forms. The majority of the MS population, 85-90%, experience a *relapsing and remitting* form (Confavreux et al., 2000). This progression is characterised by the sudden onset of new symptoms that generally remit with time, however some will have a lasting impairment on functioning (Compston & Coles, 2008; Hirst et al., 2008). Despite some impairment, the level of functioning of individuals with relapsing and remitting MS is generally stable for a number of years (Compston & Coles, 2002; Confavreux et al., 2000). After a period of 10-15 years, approximately 60% of these individuals will develop *secondary progressive* MS, which is characterised by the gradual decline in functioning (Hirst et al., 2008). In contrast, the minority of individuals diagnosed with MS, approximately 10-15% experience *primary progressive* MS (Confavreux et al., 2000). This progression course is characterised by a prolonged and gradual decline in functioning from disease onset (Compston & Coles, 2008; Mohr et al., 2004). Currently there is no cure for MS and treatment recommendations focus on symptom management (Broadley et al., 2014). This means there is a need to identify factors that exacerbate MS symptoms in order to reduce or manage these factors.

## Stress and Multiple Sclerosis

Stress is one of the most common factors thought to trigger exacerbations in MS symptoms (Heesen et al., 2007). There is no universally accepted definition of stress, however a number of different definitions conceptualise it as the cognitive and physiological experience of tension (Monroe, 2008). It is believed that stress is the result of a complex interplay between various internal and external factors. These factors include an individual's coping mechanisms, cognitive appraisals, resources, and importantly the life events they experience (Gunnar & Quevedo, 2007). Individuals with MS reportedly believe that stress can negatively affect their symptoms and trigger relapse (Brown, Tennant, Dunn, & Pollard, 2005). There is a growing body of evidence that supports this association as is highlighted by a systematic literature review and meta-analysis (Mohr et al., 2004). In this review, the results of thirteen studies each provided support for the notion that stressful life events increased an individual's risk of symptom exacerbation or relapse, and this association was clinically significant with a medium-sized effect ($d$=0.53). More recently, Artemiadis et al. (2011) conducted a systematic review that provided further support for this association. Based on these findings, it is evident there is a consistent association between experiencing a stressful life event and subsequent relapse in MS populations. It is important to differentiate between various aspects of stressful life events that may mediate this relationship, such as differences between positive and negative stressful events, the number of stressful events over a fixed time period and the duration of stressful events.

### Positive and negative stressful events & perceived severity of events.

Potential differences between the effects of positive and negative stressful life events on MS symptoms have begun to be explored (Burns, Nawacki, Kwasny, Pelletier, &

Mohr, 2014; Mohr et al., 2000). Negative stressful events are generally undesirable events that require adaptation and adjustment, whereas positive stressful events are considered desirable events that also feature the need for adjustment and thus the potential for stress (Burns et al., 2014). For example, the birth of a child may be a positive stressful event, as it does require adaptation and adjustment, but at the same time has more positive than negative connotations. Unsurprisingly, the results of these studies demonstrate that positive and negative stressful events have differing effects on MS. While stressful events perceived to be negative have been associated with an increased risk of brain lesions, an indicator of MS disease activity, events perceived to be positive have not been associated with disease activity (Burns et al., 2014; Mohr et al., 2000). Similar results have been demonstrated in naturalistic studies using relapse and brain lesions as outcomes. The results of one study, conducted over a three year period during the war between Israel and Lebanon, indicated that individuals with MS experienced significantly more relapses and brain lesions during war periods compared to non-war periods (Yamout, Itani, Hourany, Sibaii, & Yaghi, 2010). Taken together these results suggest negative stressful events, but not positive stressful events, are associated with exacerbations of MS or relapse. It is important to note that among this literature there are key differences in the way positive and negative events are categorised. In some studies events have been categorised based on desirability (Yamout et al., 2010), whereas in others they have been categorised based on the individual's perception of the event (Burns et al., 2014).

**Number of stressful events.** There have been a number of studies that have investigated how an increase in the number of stressful events experienced influences MS symptoms (Ackerman et al., 2002; Mitsonis et al., 2008; Potagas et

al., 2008). The results of these studies are inconsistent, however the majority indicate that an increase in the number of stressful events experienced also increases risk of relapse. A study conducted by Ackerman et al. (2002) followed a small sample of MS participants for one year and found that an increase in the number of stressful life events resulted in a significantly greater risk of relapse. The results of another four studies also support these findings (Mitsonis et al., 2008; Potagas et al., 2008). It must be noted that three of these studies utilised female only samples (Ackerman et al., 2002; Mitsonis et al., 2008; Potagas et al., 2008), which prevents generalisation of these results. However, similar findings were also evident in research utilising large samples of both females and males (Brown et al., 2006a, 2006b). In contrast, research by Bulijevac et al. (2003) supports the general association between stressful events increasing risk of relapse, although did not indicate a cumulative effect of the number of events further increasing the risk of relapse. Although these results are not conclusive, the majority of studies demonstrate that a greater number of stressful events increase the likelihood of a subsequent relapse.

**Duration of stressful events.** By contrast to the number of events, other researchers have examined whether the duration of a stressful event will influence the effect on MS. The results of two studies have indicated that acute stressful events, lasting less than 6 months are associated with an increased risk of relapse, whereas events with a prolonged duration of over 6 months were not significantly associated with risk of relapse (Brown et al., 2006a, 2006b). Consistent with these findings, the results of other research has demonstrated that individuals were more likely to relapse when they experienced stressful events with an acute duration of less than 2 weeks, compared to events with a prolonged duration (Ackerman et al.,

2002). Similarly, the results of a study conducted by Mitsonis et al. (2008) demonstrated that events with a duration of up to 2 weeks were associated with an increased risk of relapse. It is proposed variations between acute and prolonged durations of stressful events may be due to the individual adjusting to the stress over time. Thus an event with a prolonged duration may impact the individual less as over time the individual has adjusted to the associated stress. Although there is variability in the literature with regards to what is considered acute or prolonged duration, it is evident that acute event durations of less than 6 months significantly increase the risk of relapse.

**Overall Disease Progression**

As is evident from the above literature, there are a large number of studies that have investigated the association between stressful life events and MS relapses (Ackerman et al., 2002; Artemiadis et al., 2011; Burns et al., 2014; Mitsonis et al., 2008; Mohr et al., 2004; Potagas et al., 2008). However there are few studies that have examined the association between stressful life events and *other aspects of MS disease course*, such as anxiety, depression, and fatigue. Singularly focusing on relapses is a limited approach as relapses are a short-term outcome that do not significantly influence the irreversible disability progression of MS (Confavreux et al., 2000). Therefore, the association between stressful life events and these other aspects of MS disease course need to be investigated. Recent research has shown that anxiety, depression, and fatigue are highly comorbid among individuals with MS (Wood et al., 2012; Simpson et al., 2015). The concurrent presentation of all three outcomes occurs in a significant portion of the MS population (Wood et al., 2012) and is over three times higher than what would be expected under statistical independence (Simpson et al., 2015). These results have lead researchers to conclude

that anxiety, depression, and fatigue are part of the disease process of MS and not merely a consequence of having the disease (Wood et al., 2012; Simpson et al., 2015). Thus it is important to investigate the effect stress has on these outcome factors to extend the findings of previous research.

**Anxiety.** Anxiety refers to a negative mood state characterised by excessive fear, which is in anticipation of a real or perceived threat (APA, 2013). Anxiety is associated with a number of physiological and behavioural symptoms such as muscle tension, sweating, hypervigalence, panic, elevated heart rate, safety behaviours, and avoidance (APA, 2013). In relation to individuals with MS, research has demonstrated that anxiety is highly prevalent. It is estimated to affect 23.5 - 44.5% of the MS population (Dahl, Stordal, Lydersen, & Midgard, 2009; Janssens et al., 2006; Wood et al., 2012).

**Depression.** Depression refers to a negative mood state characterised by a low mood and diminished interest or pleasure (APA, 2013). It is associated with a variety of physical, cognitive, and behaviour symptoms. These include sleep irregularities, fatigue, problems with concentration, feelings of worthlessness, as well as unintentional weight changes (APA, 2013). Depression is prevalent among 10 - 41.8% of individuals with MS (Dahl et al., 2009; Janssens et al., 2006; Wood et al., 2012).

**Fatigue.** Fatigue has been described as the experience of extreme tiredness (Krupp, 2003), or the reversible physical and cognitive impairment that results in a lack of motivation to complete activities (Mills & Young, 2008). Researchers have suggested that fatigue experienced by those with MS is different to fatigue experienced by healthy individuals (Krupp, Serafin, & Christodoulou, 2010). MS fatigue tends to have a quicker onset, is more persistent, and prevents physical

functioning (Krupp et al., 2010). Staggeringly, results have demonstrated that fatigue is prevalent among 50-80% of individuals with MS (Lerdal, Celius, Krupp, & Dahl, 2007; Nagaraj, Taly, Gupta, Prasad, & Christopher, 2013; Wood et al., 2012).

**Rationale, Aims, and Hypotheses**

As previously stated, stress has consistently been associated with exacerbations in MS symptoms. To date, the majority of research has singularly focused on the association between stressful life events and relapses (Ackerman et al., 2002; Artemiadis et al., 2011; Burns et al., 2014; Mitsonis et al., 2008; Mohr et al., 2004; Potagas et al., 2008). Relapses are a short-term outcome that are not indicative of overall disease progression (Confavreux et al., 2000). Therefore it is necessary to explore the association between stress and other MS symptoms that have been implicated in the progression of the disease. The current study will investigate three of these symptoms, namely anxiety, depression, and fatigue (Wood et al., 2012; Simpson et al., 2015). By learning more about the association between stress and MS symptoms, this study has the potential to inform treatment recommendations and assist those with MS to manage the disease, for example using stress management interventions (Kim, 2007; Richardson & Rothstein, 2008; Salmon, 2001). Therefore the aim of this study was to build upon previous research that has established a relationship between stress and MS relapse and investigate the association between various aspects of stressful life events (e.g., number, severity, and duration) and other MS symptoms that have been implicated in the progression of the disease (e.g., anxiety, depression, and fatigue). As noted above, the results of previous research have shown that negative, but not positive, stressful life events are associated with MS relapse (Burns et al., 2014; Mohr et al., 2000). Given these findings it was hypothesised that negative stressful life events, but not positive

stressful life events would be significantly associated with higher levels of anxiety, depression and fatigue, as measured by the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) and the Fatigue Severity Scale (FSS; Krupp, LaRocca, Muir-Nash, & Steinberg, 1989), respectively. Previous research has also shown that a higher number of events (Ackerman et al., 2002), and events with an increased severity (Burns et al., 2014) are associated with increased risk of relapse. Given these findings, it was hypothesised that an increased number and severity (including readjustment weighting) of negative stressful life events (but not positive events) would be significantly associated with higher levels of anxiety, depression and fatigue, as measured by the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) and the Fatigue Severity Scale (FSS; Krupp et al., 1989), respectively. Additionally, the results of previous research have shown acute durations of less than 6 months as opposed to prolonged durations of stressful events are associated with MS relapse (Brown et al., 2006a; Mitsonis et al., 2008). Given these findings, it was hypothesised that acute duration negative stressful life events (but not positive stressful life events) would be significantly associated with higher levels of anxiety, depression and fatigue, as measured by the HADS (Zigmond & Snaith, 1983) and FSS (Krupp et al., 1989), respectively.

## Method

### Participants

The sample for this study comprised of 236 (184 females) individuals who had a first clinical diagnosis of CNS demyelination and were participating in the Ausimmune study (Lucas et al., 2007). At study entry, participants ages' ranged from 18-58 years ($M$=38.66, $SD$=9.62). The Ausimmune Study is a multicentre case-control study, which follows individuals with MS who reside within four regions of

Australia. Participants were recruited from Brisbane city, Newcastle city and surrounding areas, Geelong city and the Western Districts of Victoria, and Tasmania from the 1st of November 2003 to the 31st of December 2006. Participant recruitment involved a two-tier notification system that involved neurologists, radiologists and other relevant medical professionals practicing in the aforementioned regions. The study was conducted over a five-year period from 2003 to 2008.

**Procedure**

Prior to study commencement, ethics approval was obtained from nine regional Human Research Ethics Committees and each participant gave written informed consent. In order to be eligible to take part in the study each participant's first demyelinating event, which signifies the onset of MS, needed to be established by a neurologist. This neurological assessment occurred during the baseline interview, which also involved the completion of questionnaires and a nurse examination. Subsequent information was gathered at annual reviews from self-report questionnaires. These questionnaires included demographic information, such as age, sex, and employment status as well as medical information, such as blood pressure, and medication use. Measures of stressful life events, anxiety, depression, and fatigue were also included in these questionnaires.

**Measures.**

***Stressful life events*** were measured retrospectively at yearly intervals for five years using a stress questionnaire modified from the Social Readjustment Rating Scale (SRRS; Holmes & Rahe, 1967). The questionnaire is a self-report measure of the occurrence, severity, and duration of stressful life events that were experienced in the previous 12 months. It consists of 16 standard questions and additional space to record other events (see Appendix A). For example, indicate if "you became

pregnant or menopausal", if yes please mark the year and months this event occurred and state whether this was generally a good or bad experience. Each stressful event was rated on an eleven-point Likert scale ranging from -5 (negative stress) to +5 (positive stress). From this information individual variables were created for the number, severity (including weighting), and duration of both negative and positive events that occurred in the 5 years, 12 months, and 6 months prior to the individual's 5th year review (see Figure 1). ***The number*** of stressful events was calculated for each time period by adding the number of reported negative and positive events separately. A high score for these measures indicates the individual experienced a high number of negative or positive events for that time period. Given differences in the literature in how negative and positive events have been categorised the present study included measures for the individual's perception of the event as well as a desirability measure (readjustment weighting). ***The perceived severity*** of stressful life events was calculated for each time period by adding the Likert scale ratings for both positive and negative events separately. For example, if a participant experienced a negative event they assigned a rating of -4 and another negative event they assigned a rating of -5 they would have a severity rating for negative events of -9. Higher scores indicate the individual experienced events with a greater perceived severity, which could be either positive or negative. In order to calculate ***stress weightings*** based on desirability for each time period, the 16 standard questions and other events were organised into 33 categories that reflected themes of stressful events. Each of these categories was then assigned weightings, which indicate the amount of readjustment the event requires. These weightings were originally devised by Holmes and Rahe (1967) and later reviewed by Scully, Tosi, and Banning (2000). Higher scores indicate the individual experienced events that required a greater

amount of readjustment, which could be either positive or negative. For example the death of a family member is assigned a weight of 72.5, whereas moving house is assigned a weight of 19 (see Appendix B for a list of categories and assigned score). ***The duration*** of stressful life events was calculated for each time period by adding the duration of positive and negative events separately. Higher scores indicate the individual experienced events with a longer duration, which could be either positive or negative.

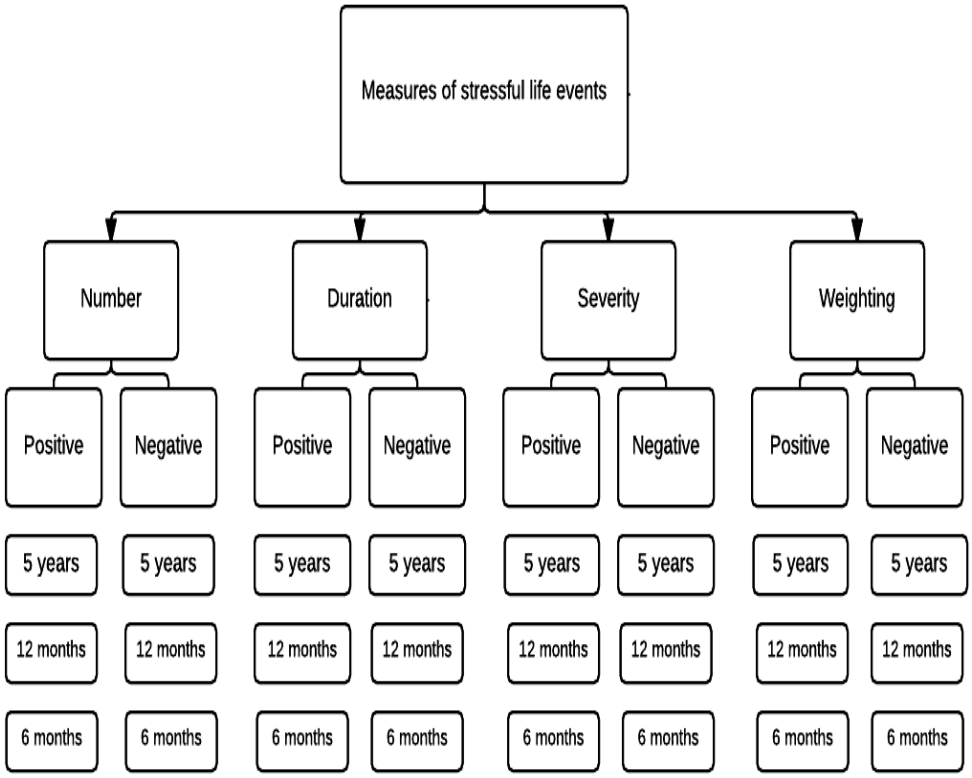


*Figure 1*: Measures of stressful life events.

**Outcome Measures.**

***Anxiety and Depression*** symptoms were measured at the fifth year review using the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983).

The HADS is a self-report measure consisting of fourteen items that are statements referring to anxiety and depression. Each item is measured on a four-point Likert scale ranging from 0 (not at all) to 3 (most of the time), for example 'I look forward with enjoyment to things' or 'I feel tense or wound up'. There are seven items that form the anxiety subscale and seven items that form the depression subscale, the scores for each seven items are added to give HADS-A and HADS-D subscale scores. Consistent with previous literature, the cut off point to define the presence of anxiety or depression was >7. Research has demonstrated that the HADS is a valid psychometric tool for use with MS populations (Honarmand & Feinstein, 2009).

***Fatigue*** was measured at the fifth year review using the Fatigue Severity Scale (FSS; Krupp et al., 1989). The FSS is a self-report measure of fatigue, which consists of nine items referring to the severity of fatigue symptoms. Each item is measured on a seven-point Likert scale ranging from 1 (disagree) to 7 (agree), for example 'I am easily fatigued' or 'fatigue causes frequent problems for me'. Higher ratings indicate higher levels of fatigue, the mean score of items produces the FSS score. Consistent with previous literature, the cut off point to define the presence of fatigue was >5.0, whereas a score of <5.0 indicates minimal or absent fatigue. The FSS was originally developed for use with MS populations and research has shown that it is a valid and reliable tool (Krupp et al., 1989).

**Other Measures.**

***Disability status*** was measured at baseline, in the second/third year review and the fifth year review using the Expanded Disability Status Scale (EDSS; Kurtzke, 1983). The EDSS provides a rating of disability that can be monitored for changes over time. The overall scores are based on assessment of impairments in eight functional systems (FS), which are pyramidal (e.g., difficulty moving limbs),

cerebellar (e.g., tremors), brainstem (e.g., speech problems), sensory (e.g., numbness), bowel and bladder function (e.g., incontinence), visual function (e.g., blurred vision), mental function (e.g., concentration), and other. Higher scores indicate a greater level of disability. Ratings on the scale range from no disability or minimal signs in one FS (1.0) to death due to MS (10.0).

***Body Mass Index*** (BMI) was measured at baseline and at the 5th year review. BMI is a common measurement used to classify weight. Scores are calculated by dividing weight by the square of height in meters ($kg/m^2$). Scores 18.5 are considered underweight, scores between 18.5 - 24.9 are classified as normal, scores between 25 - 29.9 are classified as overweight, and scores greater than 30 are classified as obese (WHO, 2015).

**Design and Data Analysis**

The current study followed a longitudinal survey design with five measurement intervals. The number, perceived severity, weighting, and duration of both positive and negative stressful life events at separate time intervals were predictor variables. There were three outcome variables: anxiety, depression and fatigue. All statistical analysis were conducted using STATA version 12.0 (StataCorp, 2015), with alpha levels set at $p < .05$. In order to examine the individual effects of the different aspects of stressful events on each outcome variable, a series of linear regressions were conducted. To obtain both unadjusted and adjusted (for control variables) estimates of the effect of each predictor on the various aspects of stress, separate linear regressions per predictor were conducted. The unadjusted linear regression provides an estimation of the effect of the outcome on the predictor variable, whereas an adjusted linear regression provides an estimation of the effect of the outcome on the predictor whilst also adjusting for important covariates that are

likely to influence the relationship. This analytic method is common in epidemiology research and has the advantage of increasing statistical power to detect effects (Kahn & Sempos, 1989; Lepage, Lamy, Dedieu, Savy, & Lang, 2015).

For each outcome measure a series of covariates were tested. Covariates were chosen for their known association with MS symptoms based on the results of Simpson et al., (2015). For anxiety, these were age, sex, disability (EDSS), and unemployment. Surprisingly, none of these variables were shown to be significant covariates of the association between the different aspects of negative stressful life events and anxiety level. Thus no adjustments were made to anxiety analyses. For depression, these were age, sex, disability (EDSS), and unemployment. Unemployment was shown to be a significant confounder of the association between the different aspects of negative stressful events and level of depression. For fatigue, these were age, sex, disability (EDSS), BMI, hypertension, immunomodulatory medications, and unemployment. Hypertension and unemployment were shown to be significant covariates of the association between the number and weighting of negative stressful events and level of fatigue

To test hypothesis one that negative (but not positive) stressful life events, would be significantly associated with anxiety, depression, and fatigue a series of simple linear regressions were conducted in which each outcome measure was individually regressed on measures of negative and positive stressful life events. To test hypothesis two that an increased number, perceived severity, and weighting of negative stressful events would be significantly associated with anxiety, depression, and fatigue a series of simple linear regressions were conducted in which each outcome measure was individually regressed on the number, severity, and weighting measures of stressful life events. To test the third hypothesis that decreased duration

of negative stressful life events would be significantly associated with anxiety, depression, and fatigue a series of simple linear regressions were conducted in which each outcome measure was individually regressed on duration measures.

## Results

### Data Assumptions and Screening

Prior to running the analyses, the distribution of the data was examined. The outcome measures of anxiety and depression were both skewed, thus in order to reduce heteroskedasticity of these measures log transformations were applied, with all means and coefficients back-transformed on the originals scales. In addition, fatigue was highly skewed subsequently cases that did not report any fatigue were removed from further analysis. The measure of fatigue, thus only includes cases that reported symptoms of fatigue. Log transformations were applied to the remaining cases with means and coefficients back transformed on the original scale.

### Sample Characteristics

The characteristics of the sample are presented in Table 1. The majority of the sample was female and currently employed, which included full time work, part time work, or home duties. At the fifth year review, over half of the sample was using immuomodulatory (anti-inflammatory) medications, a quarter of the sample was using anti-depressant medications, and a seventh of the sample was using anti-anxiety medications. Descriptive statistics for the primary and secondary outcome measures are presented in Table 2. These results demonstrate at the fifth year review participants had a mean anxiety score of 6.60, depression score of 4.14, fatigue score of 3.84 and disability score of 1.88.

Table 1

*Characteristics of Sample at 5th year review*

| Measure | | n | % |
|---|---|---|---|
| Sex | Female | 184 | 78.0 |
| | Male | 52 | 22.9 |
| Employment status | Employed | 193 | 82.1 |
| | Unemployed | 42 | 17.9 |
| Hypertension | Yes | 77 | 32.9 |
| | No | 157 | 67.1 |
| Anti-anxiety medication | Yes | 34 | 14.4 |
| | No | 202 | 85.6 |
| Anti-depressant medication | Yes | 60 | 25.4 |
| | No | 176 | 74.6 |
| Immunomodulatory medication | Yes | 127 | 53.8 |
| | No | 109 | 46.2 |

*n* = 236

Table 2

*Descriptive Statistics of Outcome Measures at 5th year review*

| Measure | *n* | *M* (*SD*) |
|---|---|---|
| Age at entry | 236 | 38.66 (9.62) |
| Age at fifth year review | 236 | 43.82 (9.58) |
| HADS – Anxiety | 219 | 6.60 (3.77) |
| HADS – Depression | 219 | 4.14 (3.40) |
| FSS | 179 | 4.93 (1.32) |
| EDSS | 229 | 1.88 (1.64) |
| BMI | 236 | 27.60 (5.75) |

**Stressful Life Events**

Descriptive statistics for measures of negative and positive stressful life events are presented in Table 3. For stressful life events that occurred in the previous 5 years, participants reported experiencing negative events in higher numbers compared to positive events. Negative stressful events were also perceived to be more severe, have a greater readjustment weighting and a longer duration compared to positive stressful events.

Table 3

*Descriptive Statistics of Stressful Life Events in past 5 years*

| Stress Measures | Negative events *M* (*SD*) | Positive events *M* (*SD*) | Total *M* (*SD*) |
|---|---|---|---|
| Number | 3.87 (3.24) | 2.94 (2.86) | 7.59 (4.92) |
| Severity | 13.72 (14.84) | 11.82 (11.58) | -* |
| Weighting | 164.04 (141.36) | 63.41 (62.48) | 250.60 (164.35) |
| Duration of events | 168.46 (249.34) | 97.08 (104.52) | 292.90 (282.80) |

(*n*=191) stress data for 191 individuals
*severity scale included zero (neutral severity) no variable created for total severity

**Associations Between Stressful Life Events and Level of Anxiety**

Table 4 shows the results of the series of linear regressions between the different aspects of negative and positive stressful life events and anxiety. Consistent with hypothesis one, measures of negative, but not positive stressful life events were significantly associated with anxiety. Also consistent with hypothesis two, increases in the number, perceived severity and weighting (readjustment score) of negative stressful life events were significantly associated with anxiety level. Interestingly, these associations were evident for negative stressful events that occurred in the previous 5 years, 12 months, and 6 months. Contrary to the assumptions in the third hypothesis, the results demonstrate that both prolonged (12 months and 5 years) and acute (6 months) duration measures were significantly associated with anxiety level.

Table 4

*Effects of Different Indicators and Intervals of Stressful Life Events on Anxiety*

| Stress Measure | | | Unadjusted | |
|---|---|---|---|---|
| | | | *B* | *SE B* |
| Number | 5 years | Total | 0.20** | 0.06 |
| | | Negative | 0.40*** | 0.09 |
| | | Positive | 0.05 | 0.11 |
| | 12 months | Total | 0.30 | 0.16 |
| | | Negative | 0.55** | 0.21 |
| | | Positive | 0.11 | 0.28 |
| | 6 months | Total | 0.38 | 0.25 |
| | | Negative | 0.70* | 0.30 |
| | | Positive | 0.13 | 0.43 |
| Severity | 5 years | Negative | -0.09*** | 0.02 |
| | | Positive | 0.00 | 0.03 |
| | 12 months | Negative | -0.18** | 0.06 |
| | | Positive | 0.02 | 0.06 |
| | 6 months | Negative | -0.23** | 0.08 |
| | | Positive | 0.03 | 0.10 |
| Weighting | 5 years | Total | 0.01*** | 0.01 |
| | | Negative | 0.01*** | 0.00 |
| | | Positive | 0.00 | 0.00 |
| | 12 months | Total | 0.01* | 0.00 |
| | | Negative | 0.01** | 0.00 |
| | | Positive | 0.01 | 0.01 |
| | 6 months | Total | 0.01* | 0.00 |
| | | Negative | 0.02** | 0.00 |
| | | Positive | 0.01 | 0.012 |
| Duration | 5 years | Total | 0.00** | 0.00 |
| | | Negative | 0.00** | 0.00 |
| | | Positive | 0.00 | 0.00 |
| | 12 months | Total | 0.01* | 0.00 |
| | | Negative | 0.02** | 0.01 |
| | | Positive | 0.01 | 0.01 |
| | 6 months | Total | 0.01 | 0.01 |
| | | Negative | 0.02* | 0.01 |
| | | Positive | 0.00 | 0.01 |

*Note *p < .05. ** p <.01. *** p < .001.*

**Associations Between Stressful Life Events and Level of Depression**

The unadjusted and adjusted coefficients for the series of linear regressions between aspects of stressful life events and depression are presented in Table 5. As predicted in hypothesis one, measures of negative, but not positive stressful life events were significantly associated with depression. Also consistent with hypothesis

two, increases in the number, severity and weighting of negative stressful life events were significantly associated with depression level. These results were evident for negative stressful events that occurred in the previous 5 years, but interestingly not for 12 months, and 6 months. Contrary with the third hypothesis, the results suggest that prolonged duration of negative events (over 5 years) were significantly associated with depression level, however there were no significant associations between acute durations of negative events (that occurred in the previous 12 months and 6 months) and depression. The results in Table 5 show these associations persisted after adjusting for employment.

**Associations Between Stressful Life Events and Level of Fatigue**

The unadjusted and adjusted coefficients for the series of linear regressions between aspects of stressful life events and fatigue are presented in Table 6. Consistent with hypothesis one, measures of negative, but not positive stressful life events were significantly associated with fatigue. Consistent with hypothesis two, the results show that measures of the number and weighting of negative stressful life events were significantly associated with level of fatigue. These associations were evident for negative stressful events that occurred in the previous 5 years, but interestingly not for 12 months, and 6 months. Contrary to the initial hypothesis, no significant associations were evident between the perceived severity of negative stressful life events and level of fatigue. The results showed no significant associations between the duration of negative stressful events and level of fatigue, which was inconsistent with the predicted effect in hypothesis three. These associations persisted after adjusting for hypertension and employment.

Table 5

*Effects of Different Indicators and Intervals of Stressful Life Events on Depression*

| Stress Measure | | | Unadjusted | | Adjusted[a] | |
|---|---|---|---|---|---|---|
| | | | *B* | *SE B* | *B* | *SE B* |
| Number | 5 years | Total | 0.03 | 0.06 | 0.03 | 0.05 |
| | | Negative | 0.21* | 0.08 | 0.17* | 0.08 |
| | | Positive | -0.12 | 0.09 | -0.07 | 0.09 |
| | 12 months | Total | -0.01 | 0.14 | -0.00 | 0.13 |
| | | Negative | 0.25 | 0.19 | 0.13 | 0.18 |
| | | Positive | -0.32 | 0.23 | -0.18 | 0.22 |
| | 6 months | Total | -0.03 | 0.21 | 0.01 | 0.20 |
| | | Negative | 0.18 | 0.27 | 0.12 | 0.25 |
| | | Positive | -0.34 | 0.34 | -0.22 | 0.34 |
| Severity | 5 years | Negative | 0.04** | 0.02 | 0.00* | 0.01 |
| | | Positive | -0.02 | 0.02 | -0.02 | 0.02 |
| | 12 months | Negative | -0.09 | 0.05 | -0.05 | 0.05 |
| | | Positive | -0.07 | 0.05 | -0.04 | 0.05 |
| | 6 months | Negative | -0.09 | 0.07 | -0.07 | 0.07 |
| | | Positive | -0.08 | 0.09 | -0.07 | 0.08 |
| Weighting | 5 years | Total | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.01** | 0.01 | 0.04* | 0.02 |
| | | Positive | -0.00 | 0.00 | -0.00 | 0.00 |
| | 12 months | Total | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Positive | -0.01 | 0.01 | -0.00 | 0.01 |
| | 6 months | Total | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Positive | -0.01 | 0.02 | -0.01 | 0.02 |
| Duration | 5 years | Total | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.00* | 0.00 | 0.00 | 0.00 |
| | | Positive | -0.00 | 0.00 | -0.00 | 0.00 |
| | 12 months | Total | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.01 | 0.00 | 0.01 | 0.00 |
| | | Positive | -0.01 | 0.01 | -0.01 | 0.01 |
| | 6 months | Total | -0.00 | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.01 | 0.01 | 0.00 | 0.01 |
| | | Positive | -0.01 | 0.01 | -0.01 | 0.01 |

*Note *p < .05. ** p <.01. *** p < .001.*

[a] *Adjusted for the effect of employment*

Table 6

*Effects of Different Indicators and Intervals of Stressful Life Events on Fatigue*

| Stress Measure | | | Unadjusted | | Adjusted[a] | |
|---|---|---|---|---|---|---|
| | | | *B* | *SE B* | *B* | *SE B* |
| Number | 5 years | Total | 0.04 | 0.02 | 0.04 | 0.02 |
| | | Negative | 0.09** | 0.03 | 0.07* | 0.03 |
| | | Positive | -0.00 | 0.01 | 0.01 | 0.03 |
| | 12 months | Total | 0.03 | 0.06 | 0.04 | 0.05 |
| | | Negative | 0.07 | 0.07 | 0.07 | 0.07 |
| | | Positive | 0.01 | 0.09 | 0.03 | 0.09 |
| | 6 months | Total | 0.04 | 0.09 | 0.04 | 0.08 |
| | | Negative | 0.10 | 0.10 | 0.09 | 0.09 |
| | | Positive | 0.06 | 0.15 | 0.05 | 0.14 |
| Severity | 5 years | Negative | -0.01 | 0.01 | -0.02 | 0.01 |
| | | Positive | -0.00 | 0.01 | -0.00 | 0.01 |
| | 12 months | Negative | -0.02 | 0.02 | -0.02 | 0.02 |
| | | Positive | -0.00 | 0.02 | 0.00 | 0.02 |
| | 6 months | Negative | -0.03 | 0.03 | -0.03 | 0.03 |
| | | Positive | 0.01 | 0.03 | 0.00 | 0.03 |
| Weighting | 5 years | Total | 0.01* | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.01** | 0.00 | 0.01* | 0.00 |
| | | Positive | 0.00 | 0.00 | 0.00 | 0.00 |
| | 12 months | Total | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Positive | 0.00 | 0.01 | 0.00 | 0.00 |
| | 6 months | Total | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Positive | 0.00 | 0.02 | 0.00 | 0.00 |
| Duration | 5 years | Total | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Positive | -0.00 | 0.00 | 0.00 | 0.00 |
| | 12 months | Total | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Positive | -0.00 | 0.01 | 0.00 | 0.00 |
| | 6 months | Total | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Negative | 0.00 | 0.00 | 0.00 | 0.00 |
| | | Positive | 0.00 | 0.01 | 0.00 | 0.00 |

*Note *p < .05. ** p <.01. *** p < .001.*

[a] *Adjusted for the effect of hypertension and employment*

## Discussion

The aim of the current study was to build upon previous research that has established a relationship between stress and MS relapse and investigate whether stress is also associated with other MS symptoms that have been implicated in the progression of the disease. Specifically, the associations between various aspects of stressful life events and anxiety, depression, and fatigue were investigated. As stress is not a uniform experience, different indicators were examined, namely the number of stressful events, the individual's perception of the events, a readjustment weighting of events, and event duration. The results of the study provided support for the initial hypothesis that negative stressful events (undesirable events that feature stress), but not positive stressful events (desirable events that also feature stress) would be associated with anxiety, depression, and fatigue. In addition, partial support was provided for the second and third hypotheses that an increased number, severity, and more heavily weighted negative events would be associated with anxiety, depression, and fatigue, and that a decreased duration of negative events would be associated with anxiety, depression, and fatigue, respectively. Taken together the results provide initial evidence that experiencing negative stressful life events is associated with the MS symptoms of anxiety, depression, and fatigue, but they also suggest that various aspects of stressful events affect these symptoms differently.

### Hypothesis One: Negative and Positive Stress

As previously mentioned, the results of the study provided support for the initial hypothesis that negative stressful events (undesirable events that feature stress), but not positive stressful events (desirable events that feature stress) would be significantly associated with anxiety, depression, and fatigue – it was found that

measures of negative stressful events were significantly associated with subsequent levels of anxiety, depression, and fatigue. Further, there were no associations between measures of positive stressful events and the outcomes. This pattern of results is consistent with previous research in this area, which has indicated associations between negative (but not positive) stressful events and exacerbations of MS or relapse (Burns et al., 2014; Mohr et al., 2000). The current finding adds to the MS literature as it extends the association between stress and relapse to anxiety, depression, and fatigue, additional MS symptoms that have been implicated in the progression of the disease, but not yet examined. The current finding also adds to research in the general population that has demonstrated negative stress increases the risk of adverse health outcomes (Cohen et al., 2012; Cohen, Tyrrell, & Smith, 1993).

Interestingly, the results also show differential temporal effects: Only long-term negative events (those that occurred in the previous 5 years) were associated with depression, but those in the past 12 months and 6 months were not. In contrast, anxiety was predicted by negative events that had occurred over all measurement points. This in interesting as it indicates experiencing a negative stressful event has a more sudden impact on anxiety compared to depression. This finding is consistent with previous research that has demonstrated that the onset of anxiety often precipitates the onset of depression (Mathew, Pettit, Lewinsohn, Seeley, & Roberts, 2011; Starr & Davila, 2012). A recently proposed model of comorbid anxiety and depression, the *diathesis anxiety model* (Cohen, Young, Gibb, Hankin, & Abela, 2014), purports that anxiety leads to depression when an individual exhibits a cognitive vulnerability to rumination and self-criticism. The model proposes that as an individual's anxiety level increases, the use of maladaptive coping mechanisms (rumination and self-criticism) also increase. Over time these coping mechanisms

lead to depressive symptoms. In the present sample it is possible that as an individual experienced stressful events, their anxiety level increased acutely. Over time the use of maladaptive coping mechanisms may have then led to increased depressive symptoms. Alternatively, when an individual experienced a stressful event that leads to anxiety, the increases in anxiety may have also led the individual to avoid activities. This avoidance may have then over time led to increases in levels of depression (Ferster, 1973; Markowitz, 2003).

**Hypothesis Two: Number, Severity, & Weighting of Stress**

The results provided partial support for the second hypothesis that qualitative and quantitative aspects of stressful life events - increased number, severity (perception of event), and weighting (readjustment score of event) of negative stressful events would be significantly associated with anxiety, depression, and fatigue. As predicted, increases in these aspects of negative events were associated with anxiety and depression, however a different pattern was evident for fatigue. Increased number and readjustment weighting of negative events were associated with fatigue, yet the perceived severity of negative events was not. These results indicate that experiencing more negative stressful life events that are perceived to be more severe, and have a higher level of readjustment (weighting) are associated with an increase in subsequent levels of anxiety and depression in those with MS. Experiencing more negative stressful life events that require a higher level of readjustment are also associated with subsequent levels of fatigue. Surprisingly, the individual's perception of the severity of negative events was not associated with subsequent fatigue. This last finding was unexpected, however it might be related to individual differences in Health Locus of Control (HLC) or the perception of control an individual has regarding their illness (Wallston, 2001; Wallston, Wallston, &

DeVellis, 1978). HLC is considered to be on a continuum from internal to external. Those with an *internal locus of control* believe that they have the means to control their health, whereas those with an *external locus of control* believe external factors control their health. External locus of control has two components, the individual's perception that *powerful others* (e.g., doctors) control their health (PHLC) and the perception that *chance or fate* control health (CHLC; Wallston, 2001; Wallston et al., 1978). In general, external locus of control is associated with poorer outcomes (Gale, Batty, & Deary, 2008), however differences are also evident between the two components of external locus of control. CHLC has been associated with higher levels of anxiety and depression (Brosschot, Gebhardt, & Godaert, 1994), whereas PHLC has been associated with higher levels of fatigue (Ray, Jefferies, & Weir, 1997). This indicates that whether an individual perceives powerful others or perceives chance to control their health has varying effects on mental compared to physical outcomes. Therefore the finding of no association between an individual's perception of severity of stressful events and fatigue may be due to underlying differences of HLC in the sample. Specifically, the sample may have exhibited higher perceptions that chance controls their MS (CHLC), which in turn might be associated with anxiety and depression but not fatigue. Additionally, an individual's health locus on control may also be related to how they perceive a stressful event. If an individual perceives chance to control their MS then they may also perceive chance to control the stressful event, which may result in higher levels of stress, and accordingly higher anxiety and depression, but not fatigue.

Aside from this one unexpected result the remaining results are as hypothesised and consistent with previous research. Specifically, previous studies have found that a greater number of negative stress events and events perceived to be

negative are significantly associated with MS relapse (Ackerman et al., 2002; Brown et al., 2006a, 2006b; Mitsonis et al., 2008; Potagas et al., 2008). The results of the current study extend these findings to other symptoms of MS implicated in the progression of the disease. The previous and current findings show that increases in the number of events, the individual's perception of the event's severity, and the level of readjustment of negative events are not only associated with relapse but also with increased anxiety, depression, and fatigue. This indicates experiencing increases in these aspects of negative stressful events may influence MS disease progression.

**Hypothesis Three: Duration of Stressful Events**

The results of this study provided partial support for hypothesis three that negative events with an acute duration (less than 6 months) would be associated with anxiety, depression, and fatigue. The results demonstrate that the duration of negative events that occurred in the previous 5 years, 12 months and 6 months were all significantly associated with anxiety. The duration of negative events that occurred in the previous 5 years, but not 12 months and 6 months, was significantly associated with depression. In addition, the results indicated there was no significant association between duration of negative events and fatigue. These findings are inconsistent with previous research in which stressful events with an acute duration were association with relapse (Ackerman et al., 2002; Brown et al., 2006a, 2006b; Mitsonis et al., 2008). The inconsistency between these results may be due to methodological differences between previous research and the current study.

The present study's finding of variations in the effect of the duration of the different outcomes can also be explained in terms of the diathesis anxiety model (Cohen et al., 2014). As previously mentioned, the model proposes that as anxiety

levels increase the use of maladaptive coping mechanisms (rumination and self-criticism) also increase. The use of these coping mechanisms over time leads to depressive symptoms. Thus in the present study experiencing negative stressful life events had an almost immediate impact on anxiety, however over time (and longer durations) experiencing stressful life events may have led to maladaptive coping mechanisms, which in turn led to depressive symptoms. The finding of no association between duration of negative events and fatigue can also be explained in terms of HLC. As discussed, the perception that chance or fate control heath has been associated with anxiety and depression (Brosschot et al., 1994), whereas the perception that powerful others (e.g., doctors) control health has been associated with fatigue (Ray et al., 1997). Again the sample may have exhibited higher perceptions that chance controls MS (CHLC), which has been associated with anxiety and depression but not fatigue. Alternatively, the perception of event duration may be more important that the absolute event duration. Therefore if an individual perceives chance to control their MS this may mean they also perceive chance to control the duration of the stressful event, which may result in anxiety and depression, but not fatigue.

To summarise, the results of this study indicate experiencing negative stressful events but not positive stressful events are associated with anxiety, depression, and fatigue. Further, experiencing more negative events, that are perceived to be more severe, have a greater readjustment rating, and are of longer duration are all associated with experiencing anxiety and depression in individuals with MS. In addition, experiencing more negative events, that have a greater readjustment rating was associated with fatigue, however the perception of severity and the duration of negative events was not associated with fatigue.

**Limitations and Directions for Future Research**

There are several strengths of the present study, including a longitudinal repeated measures design, the measurement of numerous covariates, and the statistical adjustment of these covariates. However, there are also several limitations that need to be considered when interpreting the current results. Firstly, anxiety, depression, and fatigue were only included as measures at the fifth year review. This means that the effect of stressful events over the five years could only be compared to participant's fifth year anxiety, depression, and fatigue levels. Including these measures at the same intervals as stress measurement would allow for more detailed examination of the temporal relationship between stress and these variables. Secondly, stressful life events were measured retrospectively using a self-report questionnaire, which has a number of limits. Research has shown that retrospective reporting is prone to recall errors (Dohrenwend, 2006) and that individuals are generally better able to recall severe events compared to mild events (Hardt & Rutter, 2004). Therefore severe life events (e.g., a family death) may have been more accurately recalled than mild life events (e.g., relationship issues). Self-report measures are also prone to misinterpretation as question interpretation is based on one's life experiences as well as their literacy level. This means that for different individuals the event referred to in the questionnaire may constitute a range of different meanings (Dohrenwend, 2006). This suggests the stressful event data may not be truly representative of the events that actually occurred. Additionally, the data was analysed using a series of linear regressions whereas implementing multiple regressions would have allowed the identification of which stressful life event aspects (number, severity, weighting, or duration) has the greatest influence on the outcome measures. Although using multiple regressions would have led to

interesting results the use of linear regressions was chosen in order to statistically adjust for known covariates of symptoms of MS. The current method is imperative as it results in a more power analysis.

Future research should aim to replicate the findings of this study while overcoming the aforementioned limitations. To overcome the limitations of self-report measures, interview based reports are considered the best practice in assessing stressful life events (Dohrenwend, 2006). In the present study, the stress questionnaire was implemented in an interview based format at the fourth year review, however due to time and financial constraints this format was unable to be implemented at each of the five reviews. In future research, interview based measures of stress should be utilised where possible. Future research should also aim to measure anxiety, depression, and fatigue at the same intervals as stress measurement and include multiple regression with various aspects of stress as part of the data analysis.

**Implications**

The finding that negative stressful events are associated with anxiety, depression, and fatigue in people with a first CDE has important implications for the wider MS population. There are a number of stress management interventions that have been shown to reduce the negative effects of stress (Kim, 2007; Richardson & Rothstein, 2008; Salmon, 2001). Utilising such interventions in the MS population may thus reduce the severity of anxiety, depression, and fatigue, which in turn may positively influence the progression of the disease. Treating clinicians are encouraged to provide education about stress and integrate stress management interventions into treatment recommendations. Cognitive behavioural therapy (CBT) is one psychological intervention that has been shown to be effective for the

treatment of stress (Kim, 2007; Richardson & Rothstein, 2008), as well as anxiety (Hoffman & Smits, 2008), depression (Tolin, 2010), and fatigue (Malouff, Thorsteinsson, Rooke, Bhullar, & Schutte, 2008; Price, Mitchell, Tidy, & Hunnot, 2008). CBT involves challenging and modifying maladaptive cognitions and behaviours that are believed to maintain the disorder or negative mental state. There is emerging evidence that CBT is an effective treatment for symptoms of anxiety, depression, distress, fatigue, and pain in the MS population (Thomas, Thomas, Hillier, Galvin, & Baker, 2006). Therefore CBT could be recommended as a stress management intervention for MS populations. An alternative stress management intervention is physical exercise. Exercise is increasingly being used and recommended for the treatment of stress (Pederson & Saltin, 2006; Salmon, 2001). The results of longitudinal studies have demonstrated that aerobic exercise has protective effects against stress, as well as anxiety and depression (Salmon, 2001). Similar protective effects of exercise have been demonstrated in MS populations (Pederson & Saltin, 2006).

The finding that positive stressful events are *not* associated with anxiety, depression, and fatigue in people with MS needs to be communicated to individuals with the disease. This information provides greater certainty about what factors do and do not influence MS symptoms and enables individuals to manage the disease. Greater certainty of these factors may in turn reduce psychological distress, which is common in those with MS (Janssens et al., 2006). In summary, the results of the present study show that negative stressful events are associated with anxiety, depression, and fatigue. This suggests using interventions that target stress, such as CBT or exercise, may reduce the severity of the associated symptoms, which in turn may positively affect MS disease progression. The results also show positive

stressful events are not associated with anxiety, depression, and fatigue. It is hoped this finding will provide greater certainty as to the factors that do and do not affect MS symptoms.

**Conclusions**

This five year longitudinal study expands previous research on the effect of stressful life events in those with MS as it incorporates symptoms that have been implicated in the overall progression of the disease, which were anxiety, depression, and fatigue. The results of this study led to several important conclusions. Firstly, negative stressful events, but not positive stressful events, impact subsequent levels of anxiety, depression, and fatigue in MS populations. Secondly, it was shown that individual aspects of negative stressful events affect anxiety and depression differently to fatigue. Specifically, increases in each individual aspect of negative stress (number, severity, readjustment weighting, and duration) were associated with anxiety and depression. However, increases in number and readjustment weighting of negative events were associated with fatigue, but the individual's perception of severity and duration of negative events were not associated with fatigue. The results of the study indicate the importance of integrating stress management interventions into MS treatment recommendations. As it is anticipated reducing the effects of negative stress will positively influence the progression of the disease. Further, treating clinicians are encouraged to provide education about the impact of both negative and positive stress as it is anticipated this will provide individuals with MS greater certainty about the factors that influence their symptoms. Future research should aim to replicate these findings while overcoming the limitations of the present study. Overall, this study indicates that the experience of negative stress is

not only associated with MS relapses, but is also associated with symptoms implicated in the progression of the disease.

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## STRESS

**IMPORTANT INSTRUCTIONS**

**When filling out the following form please - 1) Put one number in each box. For questions requiring you to fill in circles (eg Month) please - 2) Colour in the whole circle.**

**OFFICE USE ONLY** Nurse ID ☐☐☐

FDE/Onset Date ☐☐ / ☐☐ / ☐☐☐☐

1st Interview Date ☐☐ / ☐☐ / ☐☐☐☐

Yr 1 Annual Review ☐☐ / ☐☐ / ☐☐☐☐

Yr 2 Annual Review ☐☐ / ☐☐ / ☐☐☐☐ **or N/A** ○

2-3 Year Review Date ☐☐ / ☐☐ / ☐☐☐☐

**35.**

You have previously provided information about some of the events you experienced during the Ausimmune Study. Could you now provide some additional information by telling us more about which events you have experienced **from 12 months prior to onset of the illness that brought you into the Study until now?** *(please mark all that apply, note the year and the month, and rate the event as indicated below).*

**35a Your parent, child or partner died .....** ○ No ○ Yes | ***If YES*** ○ 1st Interview ○ 2nd Annual Review

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* -5 | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

**35b A close family friend or another relative died .....** ○ No ○ Yes | ***If YES*** ○ 1st Interview ○ 2nd Annual Review

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* | | | | | *Neither* | | | | | *Good* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | *-5* | *-4* | *-3* | *-2* | *-1* | *0* | *1* | *2* | *3* | *4* | *5* |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
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| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

**35c You yourself suffered a serious illness .....** (Other than for the study) ○ No ○ Yes | ***If YES*** ○ 1st Interview ○ 2nd Annual Review

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* | | | | | *Neither* | | | | | *Good* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | *-5* | *-4* | *-3* | *-2* | *-1* | *0* | *1* | *2* | *3* | *4* | *5* |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

| 35d You yourself suffered a serious injury or assault... | ○ No ○ Yes | *If YES* ○ 1st Interview ○ 2nd Annual Review |
|---|---|---|

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* -5 | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

| 35e A serious injury or assault happended to a close relative or friend ..... | ○ No ○ Yes | *If YES* ○ 1st Interview ○ 2nd Annual Review |
|---|---|---|

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* -5 | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

**35f You (or your parents) broke off a steady relationship .....** ○ No ○ Yes | ***If YES*** ○ 1st Interview ○ 2nd Annual Review

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* -5 | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

**35g You became pregnant or menopausal .....** ○ No ○ Yes | ***If YES*** ○ 1st Interview ○ 2nd Annual Review

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* -5 | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

**35h You became engaged, married or resumed a steady relationship.....** ○ No ○ Yes **If YES** ○ 1st Interview ○ 2nd Annual Review

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | *-5* | *-4* | *-3* | *-2* | *-1* | *0* | *1* | *2* | *3* | *4* | *5* |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

**35i You had problems with the police and a court appearance.....** ○ No ○ Yes **If YES** ○ 1st Interview ○ 2nd Annual Review

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | *-5* | *-4* | *-3* | *-2* | *-1* | *0* | *1* | *2* | *3* | *4* | *5* |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

| 35j You were sacked from your job or expelled from school..... | ○ No ○ Yes | *If YES* ○ 1st Interview ○ 2nd Annual Review |
|---|---|---|

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | *-5* | *-4* | *-3* | *-2* | *-1* | *0* | *1* | *2* | *3* | *4* | *5* |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

| 35k You had a crisis or serious disappointment in your work, school or career..... | ○ No ○ Yes | *If YES* ○ 1st Interview ○ 2nd Annual Review |
|---|---|---|

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | *-5* | *-4* | *-3* | *-2* | *-1* | *0* | *1* | *2* | *3* | *4* | *5* |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

| 35l You gained a new family member (new baby born or parent remarried)..... | ○ No ○ Yes | *If YES* ○ 1st Interview ○ 2nd Annual Review |
|---|---|---|

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* | | | | | *Neither* | | | | | *Good* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | *-5* | *-4* | *-3* | *-2* | *-1* | *0* | *1* | *2* | *3* | *4* | *5* |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

| 35m You had a major financial crisis..... | ○ No ○ Yes | *If YES* ○ 1st Interview ○ 2nd Annual Review |
|---|---|---|

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* | | | | | *Neither* | | | | | *Good* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | *-5* | *-4* | *-3* | *-2* | *-1* | *0* | *1* | *2* | *3* | *4* | *5* |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

| 35n You changed house, school or jobs ..... | ○ No ○ Yes | *If YES* ○ 1st Interview ○ 2nd Annual Review |
|---|---|---|

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | *-5* | *-4* | *-3* | *-2* | *-1* | *0* | *1* | *2* | *3* | *4* | *5* |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

| 35o You changed your personal habits, including use of alcohol or drugs..... | ○ No ○ Yes | *If YES* ○ 1st Interview ○ 2nd Annual Review |
|---|---|---|

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | *-5* | *-4* | *-3* | *-2* | *-1* | *0* | *1* | *2* | *3* | *4* | *5* |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

***NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET***

| 35p You had an outstanding personl achievement (awards, grades etc)..... | ○ No ○ Yes | *If YES* ○ 1st Interview ○ 2nd Annual Review |
|---|---|---|

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* -5 | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

*NB: IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET*

**PLEASE PROVIDE INFORMATION ABOUT OTHER EVENTS WHICH ARE NOT LISTED, OR EXTRA EVENTS ON THE FOLLOWING PAGES**

(use extra sheets if necessary)

**34q OTHER EVENTS NOT LISTED/EXTRA EVENTS** ○ No ○ Yes | ***If YES*** ○ 1st Interview ○ 2nd Annual Review

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| **Other/Extra Event type or description:** | Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | *-5* | *-4* | *-3* | *-2* | *-1* | *0* | *1* | *2* | *3* | *4* | *5* |
| _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ | 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ | 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ | 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ | 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

**IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET**

**34q OTHER EVENTS NOT LISTED/EXTRA EVENTS** ○ No ○ Yes | ***If YES*** ○ 1st Interview ○ 2nd Annual Review

***If YES ... please fill in <u>one row per event</u>. If the event occurred multiple times, please use separate row for each time it occurred. If the event CONTINUED over a period of months please use one row and mark all months in which the event was occurring.***

| **Other/Extra Event type or description:** | Year | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | *Please state whether this was generally a good or bad experience on a scale from -5 (really bad) to +5 (really good).* *Bad* *Neither* *Good* -5 | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ | 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ | 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ | 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |
| _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ | 20☐☐ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

**IF INSUFFICIENT SPACE PLEASE USE ADDITIONAL OTHER EVENTS/EXTRA EVENTS SHEET**

Appendix B

Table A7

*Weighting of Stressful Life Event Categories based on Scully et al. (2000)*

| Stressful life event category | Holmes and Rahe; and Scully et al. categories | Scully et al. weights | Final weight |
|---|---|---|---|
| Family death | Death of a spouse | 100 | 72.5* |
| | Death of a close family member | 45 | |
| Relative death | Death of a close family member | 45 | 45 |
| Participant illness | Personal injury of illness | 57 | 57 |
| Participant injury | Personal injury of illness | 57 | 57 |
| Friend injury | Change in health of family member | 46 | 46 |
| Participant breakup/issues | Divorce | 58 | 45* |
| | Marital separation | 51 | |
| | Change in number or arguments with spouse | 26 | |
| Participant pregnant | Pregnancy | 27 | 27 |
| Participant married | Marriage | 50 | 50 |
| Participant police | Minor violation with the law | 15 | 15 |
| Participant fired or expelled | Fired at work | 34 | 34 |
| Participant crisis | - | - | 55** |
| New family member | Gain of new family member | 21 | 21 |
| Financial crisis | - | - | 50** |
| Changed house | Change in residence | 19 | 19 |
| Changed health habits | Revision of personal habits | 13 | 14.3* |
| | Change in sleeping habits | 17 | |
| | Change in eating habits | 13 | |
| Personal achievement | Outstanding personal achievement | 23 | 23 |
| Change in work | Retirement | 18 | 23.5 |
| | Change to different line of work | 30 | |
| | Change in responsibilities at work | 21 | |
| | Change in work hours or conditions | 25 | |
| Work or school stress | Begin or end school | 21 | 20.3* |
| | Change in schools | 18 | |
| | Trouble with boss | 22 | |
| Family member with | - | - | 46** |

| | | | |
|---|---|---|---|
| problems | | | |
| Family member illness | Change in health of family member | 46 | 46 |
| Friend illness | Change in health of family member | 46 | 46 |
| Participant medical procedure | Personal illness of injury | 57 | 57 |
| Pregnancy issues and related | Pregnancy | 40 | 40 |
| Relationship problems with family | Trouble with in-laws | 11 | 11 |
| Family member with new relationship | Gain of new family member | 21 | 21 |
| Participant travelled | Vacation | 13 | 13 |
| Family travel or moved | Son or daughter leaving home | 18 | 18 |
| Major project or event (mostly renovations) | Change in living conditions | 26 | 26 |
| Financial related | Change in financial state | 43 | 39.5* |
| | Foreclosure of mortgage or loan | 36 | |
| Legal or business related | Business readjustment | 12 | 25.5* |
| | Minor violations with the law | 15 | |
| | Jail term | 50 | |
| Social | Change in social activities | 21 | 21 |
| Family visit stress | Change in number of family get-togethers | 21 | 21 |

*Note:*
** final weightings are based on the average weighting of multiple Holmes and Rahe categories.*
*** final weightings are the result of a comparison to similar Holmes and Rahe categories.*